

e1
Crist
oligonucleotide having a double hairpin structure with pyrimidine loops and a pharmaceutically acceptable carrier such that stable genetic modifications are made to the selected gene which result in phenotypic changes lasting beyond natural life span of differentiated epidermal cells at said locations of the human skin.

ep2
18. (Twice Amended) A method of modifying a selected gene in cells of an animal skin in vivo which comprises delivering to said cells at one or more locations of the animal skin an effective amount of a composition comprising a chimeric RNA-DNA oligonucleotide having a double hairpin structure with pyrimidine loops and a pharmaceutically acceptable carrier such that the stable genetic modifications are made to the selected gene which result in phenotypic changes lasting beyond natural life span of differentiated epidermal cells at said locations of the animal skin, wherein the animal is a mouse.

B3
32. (Twice Amended) A non-human animal model having a skin disorder at one or more locations of its skin wherein the skin disorder is a result of a treatment at said locations with a composition comprising a chimeric RNA-DNA oligonucleotide having a double hairpin structure with pyrimidine loops targeted to a selected skin gene, said oligonucleotide thereby causing a mutation in the selected skin gene which mutation leads to the skin disorder, in said animal model, and said animal model is incapable of germline transmission of the mutated gene, wherein the skin disorder is an epidermal fragility disorder, a keratinization disorder or albinism disorder.

Sub F1
ex
40. (Twice Amended) A method of correcting a mutation in a tyrosinase gene in cells of a mammalian skin in vivo which comprises delivering to said cells at one or more locations of the mammalian skin an effective amount of a composition comprising a Tyr-A RNA-DNA oligonucleotide for causing stable genetic correction in the tyrosinase gene and a pharmaceutically acceptable carrier such that the correction results in restoration of tyrosinase enzyme activity lasting beyond natural life span of differentiated epidermal cells at said locations